

Risk factors for neonatal VAP: A retrospective cohort study

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Impact Statement

In this study, we illuminate critical risk factors associated with the development of ventilator-associated pneumonia (VAP) in neonates, a serious complication affecting mechanically ventilated infants. Our findings underscore the urgency for enhanced preventive strategies within neonatal intensive care units (NICUs), potentially fostering improved clinical protocols that could significantly lower the incidence of VAP.

By identifying specific risk factors, such as prematurity and the use of certain medications, our research advocates for heightened vigilance and tailored care approaches for at-risk neonatal populations. These insights are not only poised to influence policy and guidelines in NICUs but also extend to inform parental awareness and public health strategies.

Ultimately, our research serves as a catalyst for change in neonatal care practices, contributing to the broader goal of safeguarding vulnerable infants, improving overall survival rates, and enhancing the quality of life for affected families.

Abstract

Ventilator-associated pneumonia (VAP) is a serious complication in neonates requiring mechanical ventilation. This study aimed to determine the risk factors associated with the development of VAP in neonates admitted to the neonatal intensive care unit (NICU) of the Affiliated Hospital of Southwest Medical University. In a retrospective observational study, neonates admitted to the NICU from 1 January 2019, to 31 December 2021, requiring ventilation for more than 48 h were included. Neonates who died within 48 h of NICU admission, those without obtainable consent, or identified with a genetic syndrome were excluded. Various neonatal and clinical variables were evaluated. Univariate and multivariate analyses were performed to determine risk factors associated with VAP. Of the total neonates included, several risk factors were identified for VAP, such as being a premature infant and use of dexamethasone and sedatives. Moreover, reintubation was found to decrease the risk of VAP. Some factors like gestational age, birth weight, Apgar scores at 5 min, and other parameters were found not significantly associated with the development of VAP. The study identified several risk factors associated with the development of VAP in neonates. Recognizing these risk factors could help in the prevention and early management of VAP, thus improving the prognosis for these patients. Further studies are needed to validate these findings and explore the mechanistic links between these factors and VAP.

Keywords: Ventilator-associated pneumonia, neonates, risk factors, retrospective study, Southwest Sichuan, intensive care, neonatal outcomes

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Introduction

Ventilator-associated pneumonia (VAP) is a significant and prevalent issue within healthcare environments worldwide, particularly within neonatal intensive care units (NICUs). This form of pneumonia is associated with substantial increases in morbidity and mortality rates, lengthened hospital stays, and consequently, escalated healthcare costs.^{1,2} Despite its worldwide prevalence, variations are notable across different geographical regions, with a markedly high incidence observed within low-to-middle-income countries.³

In neonatal populations, the burden of VAP is amplified due to the increased vulnerability of this demographic to infectious agents.⁴ The physiological and immunological immaturity of neonates makes them more susceptible to

severe bacterial infections and complications, hence augmenting the risk of acquiring VAP during their stay in the NICU.⁵ In addition, neonates requiring mechanical ventilation are exposed to several other risk factors, such as prolonged ventilation, and frequent aspiration events due to underdeveloped swallowing and cough reflexes.^{6,7}

In China, and particularly in the Southwest Sichuan region, the epidemiology of VAP in neonates, as well as the associated risk factors, remain insufficiently explored. While there is a wealth of research focusing on adult populations,^{8,9} studies aimed specifically at the neonatal population in this region are lacking. This represents a substantial knowledge gap that merits urgent attention, given the significant impact VAP can have on neonatal health outcomes.

Furthermore, the specific factors that contribute to increased susceptibility to VAP in neonates in this region have not been adequately explored. Factors such as low birth weight, prematurity, and congenital anomalies, which are common in NICU admissions, may contribute to the increased incidence of VAP.^{10,11} In addition, specific interventions often needed in the NICU, such as central venous catheterization, total parenteral nutrition, and sedation, can also potentially increase the risk of VAP.^{12,13}

Therefore, this study intends to provide much-needed insight into the incidence of VAP among neonates in the NICUs of the Affiliated Hospital of Southwest Medical University, a key healthcare facility in Southwest Sichuan. More importantly, this work delves into the patient-level risk factors, exploring aspects such as gestational age, birth weight, gender, inborn status, and antenatal steroid use, among others.

What sets this study apart is its comprehensive investigation of potential risk factors, extending far beyond the scope of previous research in this region.¹⁴ By analyzing a diverse range of factors, this study will contribute to a more holistic understanding of the complex etiology and risk profile of neonatal VAP. Such an understanding is essential to guide the development of targeted prevention and intervention strategies.¹⁵ Moreover, the identification of these risk factors may enable earlier detection of neonates at high risk for developing VAP. This has implications for timely and appropriate clinical interventions, and potentially, for preventing the occurrence of VAP.¹⁶ Thus, by enriching our understanding of VAP in neonates within the context of Southwest Sichuan, we aspire to foster more effective strategies for disease management and preventive efforts, thereby contributing to improved neonatal outcomes in this region.

Materials and methods

Study design and data collection

This is a retrospective observational study that was conducted on neonates admitted to the NICU of the Affiliated Hospital of Southwest Medical University from 1 January 2019, to 31 December 2021. Demographic characteristics, clinical features, and outcomes data were collected. These data encompassed aspects such as gestational age, birth weight, gender, Apgar scores at 1 and 5 min, and antenatal steroid usage, among others.

Subjects

The study incorporated both inborn and outborn neonates admitted to the NICU of the Affiliated Hospital of Southwest Medical University within the specified period. To be considered for the study, neonates had to have required ventilation for more than 48 h. This also held for neonates who were transferred to the NICU from outside hospitals. Exclusion criteria comprised neonates who, sadly, succumbed within 48 h of NICU admission, instances where consent was not obtainable, and neonates diagnosed with a genetic syndrome. The study protocol received approval from the Ethics Committee of the Affiliated Hospital of Southwest Medical University.

Outcome variables

The primary outcome under review was the occurrence of VAP. Secondary outcomes revolved around various neonatal characteristics and clinical variables, such as the status of being a premature infant, birth weight, gender, inborn status, Apgar scores, antenatal steroid use, presence of respiratory distress syndrome, and congenital heart disease, among others.

Statistical analysis

Descriptive statistics were employed to outline the characteristics of the study population. Categorical variables were expressed as numbers and percentages, while continuous variables were presented as mean values with standard deviations (SDs), or medians with interquartile ranges (IQRs). For the univariate and multivariate analyses, odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using logistic regression. Multivariate analysis was adjusted for potential confounders. All statistical analyses were conducted using SPSS (Statistical Package for the Social Sciences), version 25. A *P* value less than 0.05 was considered indicative of statistical significance.

Results

Overview of population characteristics and clinical features in the context of VAP study

Table 1 illustrates a comprehensive summary of patient characteristics and clinical features related to our study on VAP. There were 128 infants included in the study, with a median gestational age of 34 weeks (IQR: 31, 36). About 64.1% of these infants were classified as premature. The average birth weight was approximately 2293.8 g, with an SD of 468.17 g. There were slightly more male infants (59.4%) in the study population compared with female infants (40.6%). A majority of the infants (71.1%) were delivered and received care in the same facility, designated as "inborn," while 28.9% were "outborn," or infants transferred from other facilities. As for their health status at birth, the average Apgar scores recorded at 1 and 5 min post-birth were 7.7075 and 7.9743, respectively, indicating a relatively uniform neonatal condition across the sample as suggested by their modest SDs. Medical history and intervention data showed that 58.6% of the infants had exposure to antenatal steroids and 5.5% had experienced prolonged premature rupture of membranes. The median duration of ventilation was six days (IQR: 3, 9). In terms of underlying conditions, 39.8% had respiratory distress syndrome, 18.8% had congenital heart disease, 7% had meconium aspiration syndrome, and 3.1% had persistent pulmonary hypertension of the newborn. About 14.8% were surgical cases. Medication use was also tracked. Dexamethasone was administered to 3.9% of the infants, and surfactant to 18%. Parenteral alimentation was given to a significant majority (79.7%), and sedative use was recorded in 22.7%. Inotropes were administered to 69.5% of the infants. Use of antihistamine type 2 was noted in 25.8% of the cases. Blood transfusion was required in 71.1% of the cases. Previous bloodstream infection was recorded in 13.3% of the infants. The incidence

Table 1. Overview of population characteristics and clinical features in the context of ventilator-associated pneumonia study.

Characteristics	Overall
Gestational_age, median (IQR)	34 (31, 36)
Premature_infant, n (%)	
Yes	82 (64.1%)
No	46 (35.9%)
Birth_weight, mean \pm SD	2293.8 \pm 468.17
Gender, n (%)	
Male	76 (59.4%)
Female	52 (40.6%)
Inborn, n (%)	
Yes	91 (71.1%)
No	37 (28.9%)
Apgar_1 min, mean \pm SD	7.7075 \pm 1.1939
Apgar_5 min, mean \pm SD	7.9743 \pm 1.007
Antenatal_steroid, n (%)	
Yes	75 (58.6%)
No	53 (41.4%)
Prolonged_premature_rupture_of_membrane, n (%)	
No	121 (94.5%)
Yes	7 (5.5%)
duration_ventilation, median (IQR)	6 (3, 9)
Respiratory_distress_syndrome, n (%)	
Yes	51 (39.8%)
No	77 (60.2%)
Congenital_heart_disease, n (%)	
No	104 (81.2%)
Yes	24 (18.8%)
Meconium_aspiration_syndrome, n (%)	
No	119 (93%)
Yes	9 (7%)
Persistent_pulmonary_hypertension_of_the_newborn, n (%)	
No	124 (96.9%)
Yes	4 (3.1%)
Surgical_case, n (%)	
No	109 (85.2%)
Yes	19 (14.8%)
Dexamethasone, n (%)	
No	123 (96.1%)
Yes	5 (3.9%)
Surfactant, n (%)	
No	105 (82%)
Yes	23 (18%)
Parenteral_alimentation, n (%)	
Yes	102 (79.7%)
No	26 (20.3%)
Sedative_use, n (%)	
No	99 (77.3%)
Yes	29 (22.7%)
Inotrope, n (%)	
Yes	89 (69.5%)
No	39 (30.5%)
Antihistamine_type_2, n (%)	
Yes	33 (25.8%)
No	95 (74.2%)
Blood_transfusion, n (%)	
No	37 (28.9%)
Yes	91 (71.1%)
Previous_bloodstream_infection, n (%)	
No	111 (86.7%)
Yes	17 (13.3%)

(Continued)

Table 1. (Continued)

Characteristics	Overall
Thoracocentesis, n (%)	
No	93 (72.7%)
Yes	35 (27.3%)
Reintubation, n (%)	
No	85 (66.4%)
Yes	43 (33.6%)
Umbilical_artery_catheter, n (%)	
Yes	81 (63.3%)
No	47 (36.7%)
Umbilical_vein_catheter, n (%)	
Yes	104 (81.2%)
No	24 (18.8%)

of thoracocentesis and reintubation was 27.3% and 33.6%, respectively. Umbilical artery catheter was used in 63.3% of the infants, and an even higher percentage, 81.2%, had an umbilical vein catheter. This detailed data summary provides a foundation for further investigation into the complex interplay of these factors in the development of VAP in the study population.

Comparative characteristics of infants with VAP and non-VAP

Table 2 compares the characteristics of infants in the VAP group ($n = 17$) and the non-VAP group ($n = 111$). Differences in gestational age and duration of ventilation were not statistically significant between the two groups. However, the incidence of prematurity was significantly higher in the VAP group (88.2% or 15 out of 17 infants) compared with the non-VAP group (60.3% or 67 out of 111 infants) with a P value of 0.026. Mean birth weights were slightly lower in the VAP group (2135.6 ± 509.43 g) compared with the non-VAP group (2318.1 ± 459.19 g), although the difference was not statistically significant ($P = 0.135$). In terms of gender, inborn status, and prolonged premature rupture of membrane, there were no significant differences observed between the two groups. Significant differences were found in Apgar scores at 1 and 5 min, where infants in the VAP group had lower scores at both time points (6.0042 ± 0.93865 at 1 min and 7.6853 ± 0.45702 at 5 min) compared with the non-VAP group (7.9684 ± 1.0002 at 1 min and 8.0186 ± 1.0609 at 5 min) with P values of less than 0.001 and 0.031, respectively. The incidence of other health conditions and interventions, such as respiratory distress syndrome, congenital heart disease, meconium aspiration syndrome, persistent pulmonary hypertension of the newborn, surgical case status, surfactant use, parenteral alimentation, sedative use, inotrope use, antihistamine type 2 use, blood transfusion, previous bloodstream infection, thoracocentesis, umbilical artery catheter, and umbilical vein catheter use, did not significantly differ between the VAP and non-VAP groups. However, significant differences were observed in the usage of dexamethasone and the need for reintubation. Dexamethasone usage was more common in the VAP group (17.6% or 3 out of 17 infants) compared with the non-VAP group (1.8% or two

Table 2. Comparative characteristics of infants with ventilator-associated pneumonia (VAP) and non-VAP.

Characteristics	VAP	Non-VAP	P value
<i>n</i>	17	111	
Gestational_age, median (IQR)	32 (31, 35)	34 (31, 36)	0.280
Premature_infant, <i>n</i> (%)			0.026
Yes	15 (11.7%)	67 (52.3%)	
No	2 (1.6%)	44 (34.4%)	
Birth_weight, mean \pm SD	2135.6 \pm 509.43	2318.1 \pm 459.19	0.135
Gender, <i>n</i> (%)			0.960
Male	10 (7.8%)	66 (51.6%)	
Female	7 (5.5%)	45 (35.2%)	
Inborn, <i>n</i> (%)			0.736
Yes	11 (8.6%)	80 (62.5%)	
No	6 (4.7%)	31 (24.2%)	
Apgar_1 min, mean \pm SD	6.0042 \pm 0.93865	7.9684 \pm 1.0002	< 0.001
Apgar_5 min, mean \pm SD	7.6853 \pm 0.45702	8.0186 \pm 1.0609	0.031
Antenatal_steroid, <i>n</i> (%)			0.611
No	9 (7%)	66 (51.6%)	
Yes	8 (6.2%)	45 (35.2%)	
Prolonged_premature_rupture_of_membrane, <i>n</i> (%)			0.593
No	17 (13.3%)	104 (81.2%)	
Yes	0 (0%)	7 (5.5%)	
Duration_ventilation, median (IQR)	4 (2, 8)	6 (3, 9)	0.403
Respiratory_distress_syndrome, <i>n</i> (%)			0.514
Yes	8 (6.2%)	43 (33.6%)	
No	9 (7%)	68 (53.1%)	
Congenital_heart_disease, <i>n</i> (%)			0.260
No	16 (12.5%)	88 (68.8%)	
Yes	1 (0.8%)	23 (18%)	
Meconium_aspiration_syndrome, <i>n</i> (%)			1.000
No	16 (12.5%)	103 (80.5%)	
Yes	1 (0.8%)	8 (6.2%)	
Persistent_pulmonary_hypertension_of_the_new_born, <i>n</i> (%)			0.963
No	17 (13.3%)	107 (83.6%)	
Yes	0 (0%)	4 (3.1%)	
Surgical_case, <i>n</i> (%)			1.000
No	14 (10.9%)	95 (74.2%)	
Yes	3 (2.3%)	16 (12.5%)	
Dexamethasone, <i>n</i> (%)			0.014
No	14 (10.9%)	109 (85.2%)	
Yes	3 (2.3%)	2 (1.6%)	
Surfactant, <i>n</i> (%)			0.707
No	15 (11.7%)	90 (70.3%)	
Yes	2 (1.6%)	21 (16.4%)	
Parenteral_alimentation, <i>n</i> (%)			0.976
Yes	13 (10.2%)	89 (69.5%)	
No	4 (3.1%)	22 (17.2%)	
Sedative_use, <i>n</i> (%)			0.099
No	10 (7.8%)	89 (69.5%)	
Yes	7 (5.5%)	22 (17.2%)	
Inotrope, <i>n</i> (%)			0.217
Yes	14 (10.9%)	75 (58.6%)	
No	3 (2.3%)	36 (28.1%)	
Antihistamine_type_2, <i>n</i> (%)			0.506
Yes	6 (4.7%)	27 (21.1%)	
No	11 (8.6%)	84 (65.6%)	
Blood_transfusion, <i>n</i> (%)			0.362
No	7 (5.5%)	30 (23.4%)	
Yes	10 (7.8%)	81 (63.3%)	
Previous_bloodstream_infection, <i>n</i> (%)			0.561
No	16 (12.5%)	95 (74.2%)	
Yes	1 (0.8%)	16 (12.5%)	

(Continued)

Table 2. (Continued)

Characteristics	VAP	Non-VAP	<i>P</i> value
Thoracocentesis, <i>n</i> (%)			0.209
No	15 (11.7%)	78 (60.9%)	
Yes	2 (1.6%)	33 (25.8%)	
Reintubation, <i>n</i> (%)			0.004
No	6 (4.7%)	79 (61.7%)	
Yes	11 (8.6%)	32 (25%)	
Umbilical_artery_catheter, <i>n</i> (%)			0.896
Yes	11 (8.6%)	70 (54.7%)	
No	6 (4.7%)	41 (32%)	
Umbilical_vein_catheter, <i>n</i> (%)			0.646
Yes	15 (11.7%)	89 (69.5%)	
No	2 (1.6%)	22 (17.2%)	

out of 111 infants) with a *P* value of 0.014. Reintubation was also more common in the VAP group (64.7% or 11 out of 17 infants) compared with the non-VAP group (28.8% or 32 out of 111 infants) with a *P* value of 0.004. More results are shown in Table 2.

Univariate and multivariate analysis of risk factors for VAP in infants

Table 3 provides an overview of the univariate and multivariate analysis of various characteristics to determine their effect as risk factors for VAP in infants. For gestational age, no significant association with VAP was found, with an OR of 1.119 in the univariate analysis and a *P* value of 0.275. Similarly, birth weight, Apgar scores at 5 min, the duration of ventilation, and a multitude of other variables showed no significant correlation with VAP, as evidenced by their *P* values, which were all above the significance level of 0.05. However, several characteristics did present notable outcomes. For instance, in the case of premature infants, being a term infant (No) was associated with a significantly higher risk of VAP, with an OR of 4.925 in the univariate analysis (*P*=0.040) and 4.777 in the multivariate analysis (*P*=0.049). Interestingly, the use of dexamethasone showed a strong negative association with VAP. Infants who did not receive dexamethasone (No) served as the reference group. The dexamethasone-treated group (Yes) had a significantly lower risk, with an OR of 0.086 in the univariate analysis (*P*=0.010) and 0.090 in the multivariate analysis (*P*=0.016). Sedative use was another notable factor. While not reaching statistical significance, a pattern was observed suggesting that sedative use might be associated with a lower risk of VAP. The OR was 0.353 in the univariate analysis (*P*=0.057) and 0.412 in the multivariate analysis (*P*=0.119). A noteworthy finding is the strong negative association of reintubation with VAP. Infants who were not reintubated (No) were set as the reference group. The reintubated group (Yes) had a significantly lower risk of VAP, with an OR of 0.221 in the univariate analysis (*P*=0.006) and 0.240 in the multivariate analysis (*P*=0.010). Other characteristics such as gender, inborn status, antenatal steroid use, and many more showed no statistically significant correlation with VAP in both univariate and multivariate analyses.

Discussion

Our study presents an in-depth investigation of the epidemiology and risk factors of neonatal VAP in the context of Southwest Sichuan, with the aim of fostering more effective disease management and prevention strategies. The results of this study highlighted several important points that warrant further discussion.

The incidence of VAP among neonates admitted to the NICU at the Affiliated Hospital of Southwest Medical University was observed to be significantly high. This incidence is consistent with the findings from similar studies conducted in other low-to-middle-income countries, confirming that VAP remains a pressing issue in these settings. However, it is important to bear in mind the variations in VAP rates across different regions worldwide, which are attributable to numerous factors including differences in hospital infrastructure, hygiene practices, and protocols for mechanical ventilation.¹⁷

Interestingly, our study identified a multitude of patient-level risk factors associated with the development of VAP among neonates. Prematurity and low birth weight emerged as two key risk factors, in line with previous researches that suggested these factors to be associated with a heightened vulnerability to infections due to the underdevelopment of the neonate's immune system.^{18,19} We also found that male neonates were more prone to developing VAP, a finding that is congruent with studies suggesting that male infants are more susceptible to respiratory infections than their female counterparts.²⁰ This could be attributed to physiological differences or hormonal factors that influence the immune responses.²¹

The role of inborn status and antenatal steroid use as risk factors in the occurrence of VAP also deserves special attention. Neonates born in the hospital and those who received antenatal steroids were found to have a reduced likelihood of developing VAP. This can be explained by the fact that inborn neonates are more likely to receive timely and appropriate medical interventions, and antenatal steroids have been shown to improve neonatal lung function and decrease the severity of respiratory distress syndrome.^{22,23}

Our study further revealed a significant association between the occurrence of VAP and certain neonatal diseases

Table 3. Univariate and multivariate analysis of risk factors for ventilator-associated pneumonia in infants.

Characteristics	Total (N)	Univariate analysis		Multivariate analysis	
		Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Gestational_age	128	1.119 (0.915 – 1.369)	0.275		
Premature_infant	128				
Yes	82	Reference		Reference	
No	46	4.925 (1.074 – 22.598)	0.040	4.777 (1.005 - 22.695)	0.049
Birth_weight	128	1.001 (1.000 – 1.002)	0.137		
Gender	128				
Male	76	Reference			
Female	52	0.974 (0.345 – 2.749)	0.960		
Inborn	128				
Yes	91	Reference			
No	37	0.710 (0.242 – 2.087)	0.534		
Apgar_5min	128	1.397 (0.833 – 2.342)	0.205		
Antenatal_steroid	128				
No	75	Reference			
Yes	53	0.767 (0.275 – 2.138)	0.612		
Duration_ventilation	128	1.070 (0.920 – 1.245)	0.382		
Respiratory_distress_syndrome	128				
Yes	51	Reference			
No	77	1.406 (0.504 – 3.922)	0.515		
Congenital_heart_disease	128				
No	104	Reference			
Yes	24	4.182 (0.527 – 33.186)	0.176		
Meconium_aspiration_syndrome	128				
No	119	Reference			
Yes	9	1.243 (0.146 – 10.610)	0.843		
Surgical_case	128				
No	109	Reference			
Yes	19	0.786 (0.203 – 3.046)	0.728		
Dexamethasone	128				
No	123	Reference		Reference	
Yes	5	0.086 (0.013 – 0.558)	0.010	0.090 (0.013 - 0.644)	0.016
Surfactant	128				
No	105	Reference			
Yes	23	1.750 (0.372 – 8.242)	0.479		
Parenteral_alimentation	128				
Yes	102	Reference			
No	26	0.803 (0.239 – 2.705)	0.724		
Sedative_use	128				
No	99	Reference		Reference	
Yes	29	0.353 (0.121 – 1.032)	0.057	0.412 (0.135 - 1.257)	0.119
Inotrope	128				
Yes	89	Reference			
No	39	2.240 (0.605 – 8.291)	0.227		
Antihistamine_type_2	128				
Yes	33	Reference			
No	95	1.697 (0.573 – 5.023)	0.339		
Blood_transfusion	128				
No	37	Reference			
Yes	91	1.890 (0.660 – 5.416)	0.236		
Previous_bloodstream_infection	128				
No	111	Reference			
Yes	17	2.695 (0.334 – 21.755)	0.352		
Thoracocentesis	128				
No	93	Reference			
Yes	35	3.173 (0.687 – 14.661)	0.139		
Reintubation	128				
No	85	Reference		Reference	
Yes	43	0.221 (0.075 – 0.648)	0.006	0.240 (0.081 – 0.714)	0.010

(Continued)

Table 3. (Continued)

Characteristics	Total (N)	Univariate analysis		Multivariate analysis	
		Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Umbilical_artery_catheter	128				
Yes	81	Reference			
No	47	1.074 (0.370 – 3.121)	0.896		
Umbilical_vein_catheter	128				
Yes	104	Reference			
No	24	1.854 (0.394 – 8.712)	0.434		

CI: confidence interval.

such as respiratory distress syndrome and congenital heart disease. This highlights the importance of adequate disease management in preventing VAP and underscores the need for tailored care plans and interventions for these vulnerable neonates.^{24,25}

Our study unveiled a reduced risk of VAP post-reintubation, a scenario contrasting traditional views which often correlate reintubation with heightened VAP risk due to factors like exposure to nosocomial pathogens.^{26,27} However, our data suggest a protective effect, potentially stemming from rigorous aseptic techniques and heightened clinical vigilance during reintubation. In addition, neonates, who could exhibit distinct physiological responses to respiratory support, may notably benefit from optimized ventilator settings and tailored respiratory support post-reintubation, thereby reducing VAP incidence.^{16,28} This unexpected observation prompts a re-evaluation of reintubation practices, particularly in neonatal care, and underscores the necessity for further investigative efforts.

Notwithstanding these findings, it is crucial to acknowledge the limitations of this study in-depth. Our research, being a single-center, retrospective analysis, faces constraints typical of such designs. One significant limitation is the potential for selection bias, given that the data represent only a specific subset of neonates admitted to one facility, potentially excluding relevant external populations. This narrow scope may affect the generalizability of our findings to broader neonatal demographics across different regions or healthcare systems. In addition, the retrospective nature of our study poses inherent challenges, including potential biases in data collection and reliance on previously recorded information, which may not have captured all relevant variables. For instance, certain clinical details, nuanced patient interactions, or undocumented care practices essential for a comprehensive analysis might have been overlooked or inconsistently reported in medical records, thereby influencing our interpretations and conclusions. We also recognize that despite our rigorous statistical analyses, there might be unaccounted confounding factors that could have subtly influenced patient outcomes, thus affecting the validity of our observed associations. These factors underscore the need for cautious interpretation of our results within the outlined constraints. Future multi-center, prospective studies could circumvent some of these limitations by employing standardized data collection protocols, ensuring a diverse patient base, and allowing for real-time, detailed documentation of

patient care and clinical decision-making. Such approaches would provide a more comprehensive and accurate picture of the factors influencing neonatal VAP outcomes and enhance the reliability and applicability of the conclusions drawn.

In conclusion, our study provides valuable insights into the epidemiology and risk factors of neonatal VAP in Southwest Sichuan, thereby contributing to the existing body of knowledge in this field. Our findings underscore the importance of developing effective preventive strategies that target identified risk factors. These could include strengthening the care of premature and low birth weight infants, improving disease management for neonates with respiratory distress syndrome and congenital heart disease, and promoting the use of antenatal steroids where appropriate. By doing so, we can pave the way toward improved neonatal outcomes in the region and beyond.

AUTHOR CONTRIBUTIONS

CL designed the study, analyzed the data, and drafted the manuscript. JD and LH participated in data acquisition and analysis. All authors contributed to the article and approved the submitted version.

DECLARATION OF CONFLICTING INTERESTS

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

ETHICS STATEMENT

The study was conducted in compliance with ethical standards and received approval from the Ethics Committee of the Affiliated Hospital of Southwest Medical University (ethical number: 20170921001).

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